New copper-containing catalysts based on modified amorphous silica and their use in flow azide—alkyne cycloaddition*

V. A. Burilov,[a★] *A. N. Nurmukhametova,*[a] *R. N. Belov,*[a] *D. A. Mironova,*[a] *V. V. Vorob′ev,*[b] *Yu. N. Osin,*[b] *and I. S. Antipin*[a]

[a]*A. M. Butlerov Chemical Institute, Kazan (Volga Region) Federal University, 18 ul. Kremlevskaya, 420008 Kazan, Russian Federation. E-mail: ultrav@bk.ru*

[b]*Interdisciplinary Center for Analytical Microscopy, Kazan (Volga Region) Federal University, 18 ul. Kremlevskaya, 420008 Kazan, Russian Federation. E-mail: ultrav@bk.ru*

Copper-containing catalysts supported on amorphous silica modified by amines were prepared using the chemical reduction method. The morphology of copper particles and their chemical state depend on the type of the reducing agent used. The use of ascorbic acid results in the formation of monodisperse submicron Cu^0 particles 200—300 nm in size, whereas Cu^0 particles with a size ranging from 50 to 150 nm are formed when hydrazine hydrate was used. The morphology and chemical state of the copper particles reduced with sodium borohydride depend substantially on the amount of the reducing agent: Cu^0 nanoparticles 10—15 nm in size are formed if the reducing agent is an excess, layered Cu_2O plates are formed at the equimolar amount of sodium borohydride, and a decrease in the amount of sodium borohydride results in spherical Cu_2O particles. All the catalysts synthesized in the flow regime showed higher activity in the catalytic cycloaddition of azides to alkynes than the commercially available copper catalysts.

Key words: modified silica, azide—alkyne cycloaddition reaction, heterogeneous catalysis, copper nanoparticles, flow chemistry.

Copper-based materials found use in catalytic reactions of various organic compounds.[1,2] Copper and the copper systems are used in the catalytic Ullmann reactions,[3] oxidative coupling,[4,5] Cadiot—Chodkiewicz coupling,[6] Sonogashira,[7] and many other reactions. The copper-catalyzed cycloaddition of azides to alkynes (CuAAC) plays a special role.[8,9] This reaction results in the formation of 1,4-disubstituted 1,2,3-triazoles only and occurs under mild conditions in full accord with the principles of click chemistry.[10] High selectivity, mild reaction conditions, and exclusive tolerance to the presence of various functional groups are the reason for the wide use of CuAAC in diverse areas of chemistry, including organic and medical chemistry, polymer chemistry, and materials science. In addition, the CuAAC reaction is often applied for the conjugation of biomolecules with fluorescent labels.[11] The copper(I) or copper(II) salts combined with reducing agents are the catalysts of the CuAAC reactions. However, the copper nanoparticles[12—14] become more popular in catalysis in the recent decade, because, unlike homogeneous catalysis by the copper salts, these catalysts can multiply be introduced into the reaction using, in particular, possibilities of modern flow reactors.

Flow reactors have undisputable advantages over traditional batch syntheses due to efficient mixing of the components and fast heat and mass transfer.[15] In addition, the technology of back pressure control makes it possible to enhance the boiling point of the solvent and to conduct the reactions at substantially higher temperatures, which considerably accelerates the reaction.[16] To use copper nanoparticles in flow reactors, it is reasonable to immobilize the particles on the support surface. The support makes it possible to increase the total specific surface area of the catalyst and also can be a source of additional acid/base catalytic sites. Carbon materials, polymers, zinc, zirconium, aluminum, chromium, and magnesium oxides, as well as mixed oxide systems are widely used as supports for copper nanoparticles.[13] Silica and silica-based mesoporous structures can be distinguished among appropriate supports. These supports have low toxicity, reasonable

* Dedicated to Academician of the Russian Academy of Sciences I. P. Beletskaya.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 0461—0468, March, 2018.